REMARKS

In view of the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow claims 36-40, as well as newly introduced Claims 41 to 56, the only claims pending and under examination in this application.

The specification has been amended to correct obvious typographical errors in the application as filed. These errors are readily apparent from the application as a whole, as well as the claims as filed. Claims 36 and 37 have been amended to more specifically refer to the first vector as an adenoviral genome vector. Support for this amendment can be found in the abstract: "The first vector includes an adenoviral genome...." Claim 38 has been amended to correct describe the restriction endonuclease sites as first and third. Support for this amendment can be found throughout the specification, specifically on page 10, lines 28-29, and as further described below.

Newly presented Claims 41 to 56 find support in the originally filed claims.

As the above amendments introduce no new matter to the application, their entry by the Examiner is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 36-40 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. As amended, Claim 36 provides for an adenoviral genome vector, rather than a "first vector." Accordingly, the rejection to Claims 36-40 under 35 U.S.C. § 112, second paragraph, may be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 38 was rejected under 35 U.S.C. § 112, first paragraph, as failing to provide a description of a shuttle vector comprising "said first and second endonuclease sites" (Page 3, Office Action). As amended, Claim 38 provides a

description of a shuttle vector comprising "said first and **third** restriction endonuclease sites." Support for this amendment occurs throughout the specification, in particular, page 10, lines 28-29 and page 11, lines 1-6 read:

> **Flanking the insertion sequence of the second or shuttle vector are the first and third restriction sites of the first vector**. In other words, at one end of the insertion sequence of the second vector is either the first or third restriction site which is also present in the first vector. At the other end of the insertion sequence is the other of the first and third restriction sites. For example, where the first restriction site of the first vector is I-CeuI and the third restriction site of the first vector is PI-SceI, at one end of the insertion nucleic acid of the second vector is the I-CeuI site and at the other end of the insertion nucleic acid of the second vector is PI-SceI site.

Further, page 11, lines 23-26 in the specification reads:

> The first and second cleavage products are produced by contacting the first **and second vectors** with the restriction endonucleases that cleave **the first and third restriction endonuclease sites present on** these first and **second vectors**, as described above.

Further, page 20, lines 7-9 in the specification reads:

> **In addition, the subject kits may also include a shuttle vector, where the shuttle vector is characterized by including a region having the first and third restriction endonuclease sites flanking a multiple cloning site**.

These noted instances in the specification provide for a description of a shuttle vector comprising first and third restriction endonuclease sites. No new matter has been introduced. In light of these descriptions, the objection to claim 38 under 35 U.S.C. § 112, first paragraph, may be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 36, 37, 39, and 40 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Saito et al. (hereinafter "Saito") and Majumder et al.

(hereinafter "Majumder"). The Office Action asserts that it would have been obvious to one with ordinary skill in the art at the time the invention was made to use the directional cloning approach taught by Majumder in the method taught by Saito for producing recombinant adenovirus; and that Majumder teaches minimizing the occurrence of vectors that contain no insertion with use of three restriction sites. The Office Action asserts it would be obvious to package the vector containing an adenoviral genome vector, with E-region deletion and three unique restriction endonuclease sites, and corresponding restriction endonucleases into a kit. This rejection is respectfully traversed.

It is accepted that a proper prima facie obviousness rejection must be based on a combination of references that, among other requirements, teach or suggest all of the claim limitations. M.P.E.P. § 2143 states in relevant part:

> To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. **Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.**

Thus, a valid prima facie case of obviousness requires a teaching or suggestion by the combined references of each and every limitation of the claimed invention.

In the present case, the combined teaching of Saito and Majumder fails to teach or suggest all of the limitations of the claimed invention. Specifically, these the kit of claims 36, 37, 39 and 40 require at least the following two components:

(1) an adenoviral genome vector comprising an E gene deletion and three unique, restriction endonuclease sites located in the E gene deletion, where the sites do not occur in the wild type adenoviral vector genome; and

(2) the three endonucleases corresponding to the sites of the vector.

The references cited in the Office Action fail to teach or suggest assembly of a kit that includes these specified components.

As summarized above, the rejection is based on the combination Saito's disclosure of an adenoviral vector with Majumder's background-minimized cassette mutagenesis by PCR (BMCM-PCR) method.

Majumder's BMCM-PCR method is summarized in Figure 1 of the paper and is reproduced below:

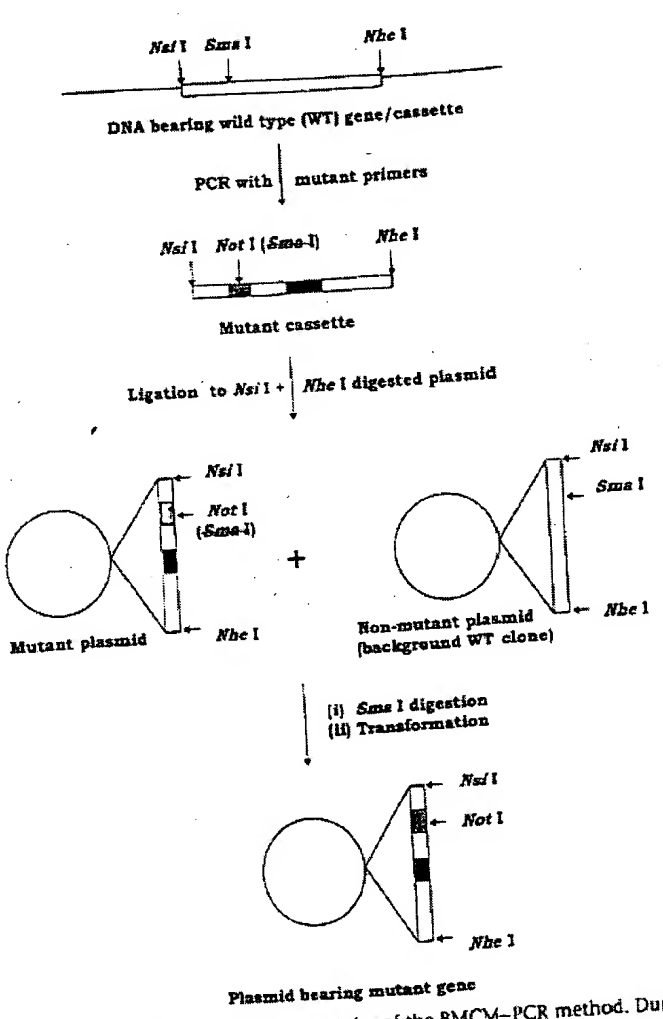

FIGURE 1 A graphic presentation of the principles of the BMCM–PCR method. During the PCR-

The method suggested by the combined teaching of Majumder and Saito would be to introduce the product of the first mutant generation step of the Majumder method into the Saito vector by directional cloning. Specifically, one would ligate the mutant cassettes produced by Majumder's first "PCR with mutant primers" step into *Nsi* I and *Nhe* I digested Saito adenoviral vector. In other words, Figure 1 reproduced above would be modified such that the Saito's adenoviral vector is vector into which the mutant cassette is ligated.

If one were to sell a combination of reagents, e.g., in a kit form, to practice this method which is suggested by Majumder in view of Saito, one would sell Saito's vector with *Nsi* I and *Nhe* I sites in the E-gene deletion region, and *Nsi* I and *Nhe* I.

One would not sell a third restriction endonuclease because one would not know what specific DNA sequence a given user would be interested in studying, and thus one would not know what site would be in that sequence and available for mutation.

One would also not sell an adenoviral vector that includes "an E gene deletion region and first, second and third restriction endonuclease sites, wherein each of said first, second and third restriction endoncuclease sites are: (i) different, (ii) do not occur in the corresponding wild type adenoviral genome and (iii) are located in said E gene deletion region" since the vector would only have two sites in the E-gene deletion region, i.e., the *Nsi* I and *Nhe* I sites.

As such, the combined teaching of Saito in view of Majumder fails to teach or suggest all of the elements the claims kits. Accordingly, the rejection of Claims

36, 37, 39, and 40 under 35 U.S.C. § 103(a) as being unpatentable over Saito in view of Majumder may be withdrawn.

With respect to new Claims 41 to 43, these claims are also patentable over the cited references of record for at least the reasons discussed above.

Finally, with respect to new Claims 44 to 56, all of these claims include the element of Claim 38, which was not included in any rejection based on prior art. As such, these claims are also patentable over the art of record.

CONCLUSION

In view of the above remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance.

If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided. The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815.

Respectfully submitted,
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